

Ab Initio Conformational Analysis of Cyclooctane Molecule

WILLIAN R. ROCHA, JOSEFREDO R. PLIEGO, JR., STELLA M. RESENDE, HÉLIO F. DOS SANTOS, MARCOS A. DE OLIVEIRA, WAGNER B. DE ALMEIDA*

Laboratório de Química Computacional e Modelagem Molecular (LQC-MM),
Departamento de Química, ICEx, UFMG, Belo Horizonte, MG, 31270-901, Brazil

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ABSTRACT: The potential energy surface (PES) for the cyclooctane molecule was comprehensively investigated at the Hartree–Fock (HF) level of theory employing the 3–21G, 6–31G, and 6–31G* basis sets. Six distinct true minimum energy structures (named B, BB, BC, CROWN, TBC, and TCC₁), characterized through harmonic frequency analysis, were located on the multidimensional PES. Two transition state structures were also located on the PES for the cyclooctane molecule. Electron correlation effects were accounted for using the Møller–Plesset second-order perturbation theory (MP2) approach. The predicted global minimum energy structure on the *ab initio* PES for the cyclooctane molecule is the BC conformer. A gas phase electron diffraction study at 300 K suggested a conformational mixture while an NMR study in solution at 161.5 K predicted the BC conformer as the predominant form. The equilibrium constants reported in the present study, which were evaluated from the *ab initio* calculated total Gibbs free energy change values, were in good agreement with both experimental investigations. The *ab initio* results showed that the low temperature condition significantly favored the BC conformer while above room temperature both BC and CROWN structures can coexist. © 1998 John Wiley & Sons, Inc. J Comput Chem 19: 524–534, 1998

Keywords: *ab initio* conformational analysis; cyclooctane molecule; potential energy surface; Hartree–Fock theory; Møller–Plesset theory

*Present address: Quantum Theory Project, University of Florida, 362 Williamson Hall, Gainesville, FL 32611-8435 (unit 1/98)

The Grupo de Química Computacional, e Modelagem Molecular dedicate this article to the memory of our estimable colleague Professor Milton Francisco de Jesus Filho.

Correspondence to: W. B. De Almeida; e-mail: wagner@metumo.qui.ufmg.br

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Introduction

The conformational analysis of saturated cyclic compounds has been of great interest to chemists since the 19th century. The intramolecular interactions that take place in the ring systems are more difficult to understand than the ones occurring in acyclic compounds. A great variety of methods have been utilized for the determination of the geometries and relative energies of cyclic compounds. The cyclooctane molecule belongs to the class of average cycles having a very complex multidimensional potential energy surface (PES), and a definitive analysis of the conformations adopted by this cyclic hydrocarbon has been particularly challenging. The molecular structure of the cyclooctane molecule has been widely discussed since 1960. The central point of the discussion was the conformation adopted by this molecule when studied by a variety of experimental methods. Hendrickson,¹ who did a pioneer work, reported nine conformations of the cyclooctane molecule that belong to three families: CROWN, BOAT-BOAT (BB), and BOAT-CHAIR (BC), as shown in Figure 1. According to Hendrickson, interconversions between members of different families are certainly possible, so the cyclooctane

will then form a conformational mixture with great mobility at ordinary temperatures in the gas phase. A previous electron diffraction study² of cyclooctane in the gas phase at 40°C was in good agreement with Hendrickson's suggestion. At the same time X-ray diffraction experiments carried out for derivatives of cyclooctane showed that, in the crystal, the BC conformer is certainly the preferred one,³ although there is a propensity for adopting the CROWN conformation. Following this report, a series of additional indications were also obtained in favor of the predominant existence of the BC conformer in the liquid state and gas phase. Anet and Basus⁴ reported an investigation of the ¹H NMR spectrum, showing that the cyclooctane exists predominantly in the BC form with a small fraction (6% at room temperature) of the other conformations in the CROWN family. Pakes et al.⁵ reported an analysis of the infrared and Raman spectrum of liquid and gas phase cyclooctane, and the low frequency vibrations of the ring were consistent with the existence of only the BC conformer. The favoritism of the BC conformer was also reported more recently by Dorofeeva et al.⁶

Stochastic or Monte Carlo methods combined with analytical minimization techniques to explore the molecular mechanics (MM2) energy surface of cyclic hydrocarbons was used in the late 1980s by Saunders⁷ and Still and colleagues⁸ to study the preferred conformations of the cyclooctane molecule and the conformers' population at room temperature. Following this work, Ferguson and Raber used a Monte Carlo type sampling routine called random incremental pulse (RIPS)⁹ combined with the MM2 program that contains a metal-extended force field (MM2MX)¹⁰ for locating local as well as global minima on the PES for the cyclooctane molecule.⁹ They found that the BC is the global minimum and six other conformers named B, BB, CROWN, CC, TCC, and TBC were predicted to be local minima. Cyclooctane was further investigated by Ferguson et al.¹¹ using the MM2MX, AM1, and Hartree-Fock (HF)/3-21G methodologies. They found the BC conformer as the global minimum and the other six structures reported in ref. 9 as stationary points on the PES. Ferguson et al. did not perform harmonic frequency analysis to characterize the located stationary points as minima or transition state structures.¹¹ In all studies reported so far, the conformational analysis was not fully addressed in order to bring the separate experimental observations into agreement.

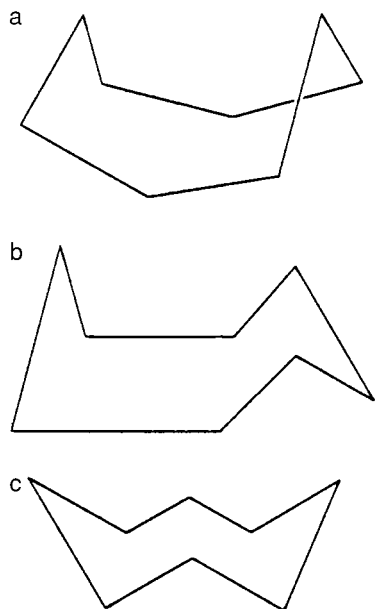


FIGURE 1. The three representative families of cyclooctane conformations: (a) BB family, (b) BC family, and (c) CROWN family.

In this study, we investigated the PES for the cyclooctane molecule, employing standard *ab initio* methods. We sought to locate the possible equilibrium structures, their relative stability, and the transition state (TS) structures involved in the conformational interconversion pathways. Because there were no direct experimental geometrical parameters available for the TS structures, the theoretical values reported here can be regarded as the best available data for this cyclic hydrocarbon. *Ab initio* harmonic frequency calculations were performed for an unambiguous characterization of the stationary points located on the multidimensional PES. Through the calculation of thermodynamic properties as a function of the temperature, the equilibrium constants for various conformation interconversions were systematically evaluated, and this provided an understanding of the experimental reports on the conformational analysis of the cyclooctane molecule.

Calculations

An extensive search for stationary points on the PES for the cyclooctane molecule was carried out by first using a random routine in connection with the MMX force field.¹² Subsequently several distinct trial atomic spatial arrangements were used in the geometry optimization jobs, using *ab initio* HF methods to locate all of the possible equilibrium structures present on the multidimensional energy surface. Six true minima (B, BB, BC, CROWN, TBC, and TCC₁) were characterized through harmonic frequency analysis and were located on the *ab initio* PES employing the 3-21G,¹³ 6-31G,¹⁴ and 6-31G* (ref. 14) basis sets. Two TS structures connecting the BC, CROWN, and TBC minima were also located and the respective geometries were fully optimized using a proper routine for locating TS structures. Electron correlation effects were accounted for using the Møller-Plesset second-order perturbation theory (MP2) treatment on single point calculations at the fully optimized HF geometries. This is a less expensive computational procedure that has been successfully applied for the 1,5-cyclooctadiene (COD) molecule.¹⁵ A more extended basis set of triple zeta quality, 6-311G*,¹⁶ was also used in the MP2 calculations. Full MP2/6-31G* geometry optimizations were carried out for the global minimum BC structure and the next important local minimum, the CROWN conformer. The *ab initio*

calculations were performed with the GAMESS package¹⁷ as implemented on a Sun Ultra-1 and Silicomgraphics Indigo-2 R10000 workstations at the Laboratório de Química Computacional e Modelagem Molecular, Departamento de Química, Universidade Federal de Minas Gerais.

Results and Discussions

The *ab initio* calculated torsion angles for the six minimum energy (true) structures and two TS structures located on the PES for the cyclooctane molecule are given in Table I. Table II gives the respective relative total energies. The HF/6-31G* fully optimized structures located on the PES for the cyclooctane molecule are depicted in Figures 2-4; Figures 3 and 4 also show the conformational interconversions. It can be seen from Table I that there is an overall agreement between the empirical and quantum mechanical calculations regarding the torsion geometrical parameters for the global minimum and local minima. The fact that the fully optimized MP2 geometries are fairly close to the HF/6-31G* ones is a particularly useful result. This shows that a single point MP2 calculation at the fully optimized HF/6-31G* geometry is indeed a trustable and computationally cheaper procedure for including electron correlation effects in conformational analysis studies. Bond distances and bond angles did not vary significantly within the six conformers reported in Table I, so they are omitted here.

For the CROWN conformer the 3-21G basis set produced some conflicting geometrical parameter results. Table I shows that two distinct CROWN conformations are obtained with the 3-21G basis set. The distorted CROWN conformer, shown in brackets, is located when the respective MM2 structure is used as the initial guess in the HF/3-21G geometry optimization. The proper CROWN minimum is found when the HF/6-31G* respective minimum is used as the initial guess in the HF/3-21G geometry optimization job. The 6-31G and 6-31G* basis sets always lead the optimization to the expected CROWN structure. It seems that the 3-21G basis set sometimes locates rather unreal minima and so it may not be adequate for determining the structure of cyclic compounds with a high degree of structural flexibility. When we tried to reoptimize the previously reported CC and TCC structures, the same situation happened. These results are in Table III. The CC

TABLE I.
Ab Initio Ring Dihedral Angles for Six True Minima (B, BB, BC, CROWN, TBC, TCC₁) and First-Order Transition State Structures (TS₁, TS₂) Located on PES for Cyclooctane Molecule.

Angles and Degrees	B	BB	BC	CROWN	TBC	TCC ₁	TS ₁	TS ₂
[C ₁ , C ₂ , C ₃ , C ₄]								
HF/3-21G	37.15	-53.01	-67.1	-86.3 [-105.98] ^a	-86.95	50.43	-35.63	-73.44
HF/6-31G	39.58	-52.30	-66.50	-84.78	-84.40	51.45	-36.27	-71.73
HF/6-31G*	45.15	-52.05	-60.55	-83.76	-81.90	51.87	-36.44	-70.71
MP2/6-31G*			-65.15	-84.31				
Others ^b	34.1 (34.5)	51.5 (51.6)	-67.9 (67.7)	-88.4 (87.8)	-91.5 (89.0)			
[C ₂ , C ₃ , C ₄ , C ₅]								
HF/3-21G	-65.68	-51.96	67.17	85.6 [84.92] ^a	92.24	-92.06	76.61	81.52
HF/6-31G	-62.52	-51.31	66.50	84.79	90.81	-90.76	76.17	80.09
HF/6-31G*	-57.51	-51.09	65.55	83.76	89.63	-89.66	75.82	79.11
MP2/6-31G*			65.15	84.31				
Others ^b	-66.6 (64.8)	-51.5 (51.6)	67.9 (67.7)	88.4 (87.8)	92.7 (92.2)			
[C ₃ , C ₄ , C ₅ , C ₆]								
HF/3-21G	-37.23	52.92	-102.36	-86.0 [-66.86] ^a	-50.58	87.14	-115.29	-75.67
HF/6-31G	-39.68	52.24	-100.48	-84.05	-51.25	84.06	-112.89	-75.60
HF/6-31G*	-45.34	52.00	-99.61	-83.03	-51.83	81.90	-111.55	-75.05
MP2/6-31G*			-100.74	-83.60				
Others ^b	-34.1 (34.5)	51.5 (51.6)	-101.6 (101.7)	-88.4 (87.8)	-48.0 (49.5)			
[C ₄ , C ₅ , C ₆ , C ₇]								
HF/3-21G	65.66	51.87	44.19	86.7 [85.10] ^a	-46.48	-92.54	30.55	-10.60
HF/6-31G	62.44	51.26	43.53	84.05	-45.09	-90.76	30.09	-9.13
HF/6-31G*	57.91	51.08	43.60	83.03	-44.39	-89.65	29.20	-9.01
MP2/6-31G*			44.35	83.61				
Others ^b	66.6 (64.8)	51.5 (51.6)	43.9 (43.6)	88.4 (87.8)	-47.6 (46.6)			
[C ₅ , C ₆ , C ₇ , C ₈]								
HF/3-21G	37.28	-52.70	65.55	-86.3 [-105.98] ^a	118.87	50.15	23.59	99.06
HF/6-31G	39.86	-52.11	64.48	-84.79	114.96	51.46	23.95	96.47
HF/6-31G*	44.93	-51.94	63.90	-83.76	113.62	51.86	24.96	95.64
MP2/6-31G*			64.93	-84.31				
Others ^b	34.1 (34.5)	-51.5 (51.6)	63.8 (64.8)	-88.4 (87.8)	117.1 (117.3)			
[C ₆ , C ₇ , C ₈ , C ₁]								
HF/3-21G	-65.67	-52.09	-65.56	85.6 [84.92] ^a	-46.80	47.24	30.84	-51.67
HF/6-31G	-62.52	-51.39	-64.50	84.80	-45.12	44.98	29.91	-51.18
HF/6-31G*	-57.52	-51.14	-63.91	83.76	-44.39	44.37	29.18	-50.92
MP2/6-31G*			-64.93	84.32				
Others ^b	-66.6 (64.8)	-51.5 (51.6)	-63.8 (64.8)	88.4 (87.8)	-48.2 (46.6)			
[C ₇ , C ₈ , C ₁ , C ₂]								
HF/3-21G	-37.38	52.81	-44.18	-86.0 [-66.85] ^a	-50.49	-119.09	-115.51	-58.54
HF/6-31G	-39.98	52.18	43.51	-84.05	-51.24	-114.89	-112.72	-57.64
HF/6-31G*	-45.11	51.96	-43.58	-83.03	-51.84	-113.55	-111.54	-57.40
MP2/6-31G*			44.34	-83.61				
Others ^b	-34.1 (34.5)	51.5 (51.6)	-43.9 (43.6)	-88.4 (87.8)	-47.7 (49.5)			
[C ₈ , C ₁ , C ₂ , C ₃]								
HF/3-21G	65.86	52.17	102.35	86.7 [85.10] ^a	92.40	46.41	76.55	102.24
HF/6-31G	62.84	51.44	100.47	84.04	90.84	44.98	76.16	99.92
HF/6-31G*	57.58	51.18	99.62	83.03	89.63	44.36	75.82	98.88
MP2/6-31G*			100.74	83.61				
Others ^b	66.6 (64.8)	51.5 (51.6)	101.6 (101.7)	88.4 (87.8)	93.1 (92.2)			

TS₁ and TS₂ probably interconvert the BC, CROWN, and TBC conformers.

^a A distorted CROWN local minimum located only on the HF/3-21G PES.

^b Value obtained using a fitted empirical potential function from ref. 18. The values in parentheses are the MM2 dihedral angles from ref. 9.

TABLE II.
***Ab Initio* (HF, MP2) Energy Differences (kcal / mol) for True Minimum Energy Structures on PES for Cyclooctane Molecule.**

	B	BB	BC	CROWN	TBC	TCC ₁	TS ₁	TS ₂
Empirical value ^a	2.88	4.03	0.0	0.86	1.70			
MM2 value ^b	3.10	3.51	0.0	1.13	1.64			
HF / 3–21G	3.95	4.31	0.0	1.72 (1.65) ^c	1.83	1.83	12.16	3.02
HF / 3–21G(ZPE corrected)	4.09	4.43	0.0	1.20	1.70	1.70		
HF / 6–31G	3.99	4.12	0.0	0.72	1.74	1.74	11.78	2.81
HF / 6–31G(ZPE corrected)	4.12	4.20	0.0	0.18	1.62	1.63		
HF / 6–31G*	3.55	3.56	0.0	0.53	1.92	1.92	11.95	2.93
HF / 6–31G*(ZPE corrected)	3.70	3.71	0.0	0.032	1.80	1.80		
MP2 / 6–31G // 6–31G	3.29	3.45	0.0	2.10	1.79	1.80	11.67	3.07
MP2 / 6–31G // 6–31G(ZPE corr.)	3.42	3.59	0.0	1.56	1.67	1.69		
MP2 / 6–31G* // 6–31G	3.27	3.50	0.0	2.03	1.95	1.94	12.09	3.16
MP2 / 6–31G* // 6–31G(ZPE corr.)	3.40	3.64	0.0	1.49	1.83	1.83		
MP2 / 6–31G* // 6–31G*	3.40	3.49	0.0	1.99	1.97	1.97	12.15	3.20
MP2 / 6–31G* // 6–31G*(ZPE corr.)	3.55	3.60	0.0	1.49	1.85	1.85		
MP2 / 6–311G* // 6–31G*	3.10	3.49	0.0	2.22	1.85	1.85	11.64	3.04
MP2 / 6–311G* // 6–31G*(ZPE corr.)	3.28	3.64	0.0	1.72	1.73	1.73		
MP2 / 6–31G*			0.0	2.20				
MP2 / 6–311G* / MP2 / 6–31G*			0.0	2.37				

TS₁ and TS₂ structures are first-order transition states probably connecting the process CROWN ⇌ BC ⇌ TBC, so the respective energy difference is the conformational interconversion energy barrier. ZPE stand for the zero-point energy correction evaluated with scaled (0.89) HF harmonic frequencies.

^a Empirical values obtained using a fitted empirical potential function from ref. 18.

^b MM2 empirical value from ref. 9.

^c HF / 3–21G value for the distorted CROWN structure reported in Table I, which is not a local minimum on the HF / 6–31G and HF / 6–31G* PES.

and TCC conformers do not exist on the HF/6–31G* PES. They only exist on the AM1 and HF/3–21G less accurate PES. It can be seen from Table III that the MM, semiempirical, and HF/3–21G approaches all predicted a similar geometry for the CC and TCC conformers. However, the HF/6–31G* calculations revealed that these structures do indeed optimize to the well-known CROWN conformer. This can be understood on the basis that the CC and TCC are very flat minima on the HF/3–21G PES, and at a higher level of calculation these minima just disappear. In the light of these results, it can be said definitely that the six minimum energy structures predicted in the HF/6–31G* calculations reported here are the possible stable minima on the PES for the cyclooctane molecule. The previous reported CC and TCC structures are just artifacts of the theoretical treatment used for generating the quantum mechanical PES. Therefore, the conformation interconversions must take place among the B, BB, CROWN, BC, TBC, and TCC₁ conformers. It should also be said that the TCC₁ conformer located in the present

work was never mentioned before and was overlooked in all previous calculations. The TCC conformer showed in Table III was previously predicted to exist, but the present calculation showed that this structure optimizes to the CROWN conformer.

The total energies relative to the glow minimum BC structure are reported in Table II. When reading Table II, the importance promptly emerges of electron correlation for evaluating relative energies of different conformers of the cyclooctane molecule. It can be seen that an adequate treatment of electron correlation is crucial in establishing the energetic order of the BC and CROWN conformers using *ab initio* methods. The HF/6–31G and HF/6–31G* relative energies differ considerably from the MP2 calculated energies, and so the HF level of theory cannot be trusted for predicting relative energies of distinct conformers. On the other hand, the MM2 relative energies are in very satisfactory agreement with our best *ab initio* results (MP2/6–311G* // 6–31G*, plus zero energy correction).

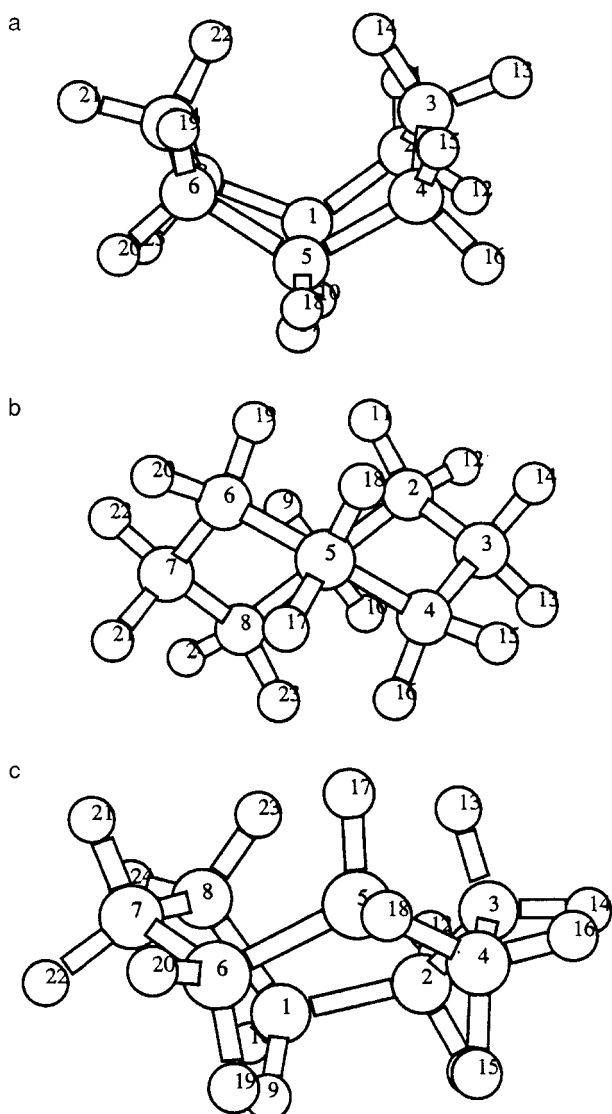


FIGURE 2. The HF/6-31G* fully optimized minimum energy structures located on the PES for the cyclooctane molecule: (a) B, (b) BB, and (c) TCC₁.

It is interesting to point out that the HF/3-21G relative energy calculations for the BC and CROWN conformers are somehow closer to the MP2/6-31G* respective results than the HF/6-31G and HF/6-31G* ones (see Table II). It should be said that the 3-21G basis set in various other situations produced very satisfactory results, and the reason for this may be a kind of error cancellation. However, caution is needed as far as cyclic flexible structures are concerned when using the 3-21G basis set. As shown in this article, it may lead the geometry optimization process to a spatial

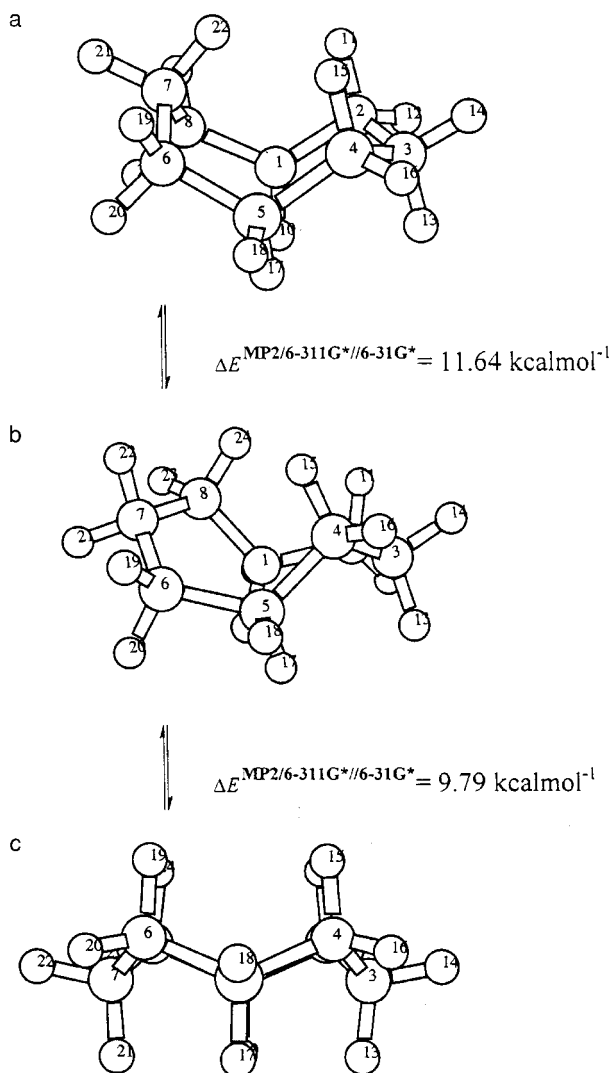


FIGURE 3. The HF/6-31G* fully optimized global minimum energy structure, BC, the local minimum, CROWN, and a transition state structure, TS₁. The MP2/6-311G*//6-31G* energy barrier for conformational interconversion is given. The TS₁ structure is shown to connect the two minima on a minimum energy path on the PES for the cyclooctane molecule. (a) BC, (b) TS₁, (c) CROWN.

arrangement that is very distorted compared to the one predicted by extended basis sets.

Table IV reports the *ab initio* total Gibbs free energy difference (ΔG^{TOT}) in relation to the BC global minimum structure evaluated at distinct temperatures. The ΔG^{TOT} values are calculated with the expression below, where the subscripts TRANS, ROT, VIB, and ELECTRONIC refer to translation, rotational, vibrational, and electronic

contributions to the Gibbs free energy function, respectively.

$$\Delta G^{\text{TOT}} = \Delta G_{\text{TRANS}} + \Delta G_{\text{ROT}} + \Delta G_{\text{VIB}} \\ + \Delta E(\text{electronic} + \text{nuclear repulsion}).$$

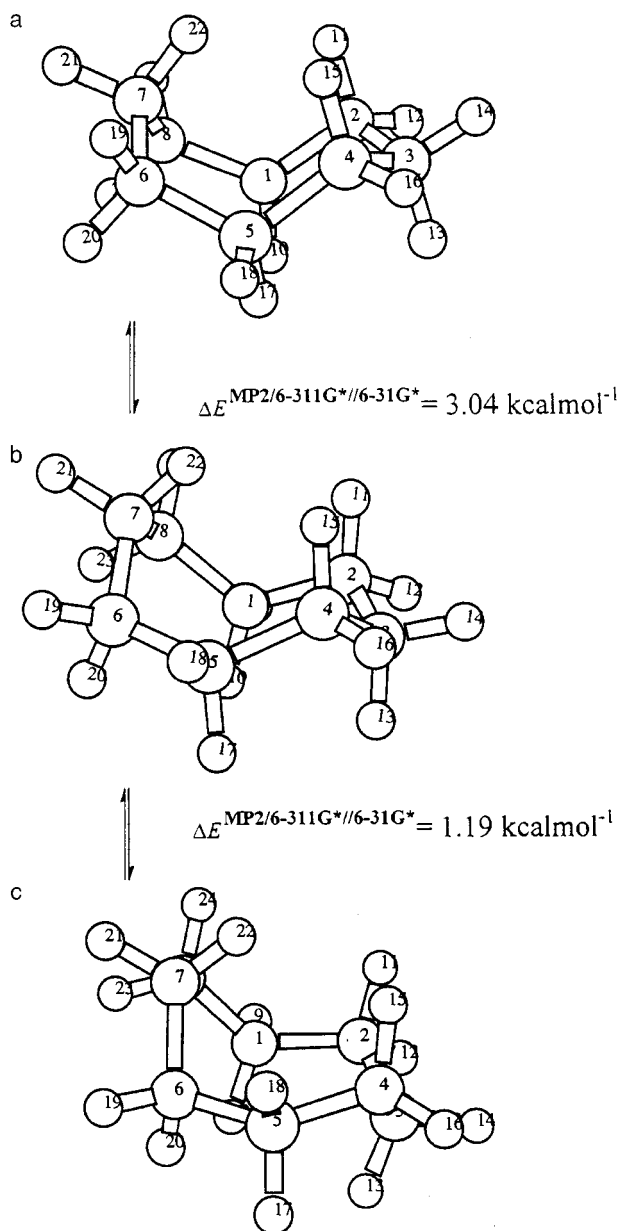


FIGURE 4. The HF/6-31G* fully optimized structure of the local minimum TBC and another transition state structure. The conformational interconversion process $\text{BC} \rightleftharpoons \text{TBC}$, through TS_2 , is shown along with the MP2/6-311G*//6-311G* energy barrier. (a) BC, (b) TS_2 , (c) TBC.

The HF/6-31G* calculated harmonic frequencies, scaled by the recommended factor of 0.8,¹⁹ were used for the partition functions evaluation. The striking difference between the HF and MP2 results is quickly seen, and electron correlation is shown to play an important role in the evaluation of ΔG^{TOT} values. The percent concentration of each conformer located on the PES for the cyclooctane molecule calculated from the *ab initio* equilibrium constants ($K_{\text{eq}} = \exp[-\Delta G/RT]$) for distinct temperatures are given in Table V. The HF/6-31G and HF/6-31G* results for the BC and CROWN conformers are in total disagreement with the MP2 values. This shows that the HF level of calculation is not sufficient for the prediction of equilibrium constants for these cyclic hydrocarbons. Again the HF/3-21G results for the BC and CROWN conformers are in line with the MP2 predictions, which may be due to an error cancellation. Therefore, we concentrate our discussion on the MP2 results.

Table V shows that the BC and CROWN conformers are the most probable ones to be found at the range of temperatures investigated, followed by the TBC and TCC_1 conformers. The B and BB conformers have a negligible proportion at equilibrium. Increasing the basis set to a triple zeta level did not significantly alter the observed trend. At 161.5 K or lower temperatures the BC conformer is predominant and only traces of the CROWN conformer up to 4% can be observed. At room temperature or even higher temperatures, the CROWN conformer is competing with the global minimum BC structure. At 313.15 K a mixture containing 62% BC, 23% CROWN, and 6% TBC and TCC_1 is predicted to exist (at the MP2/6-311G*//6-31G* level of calculation). Our *ab initio* results are in straightforward agreement with the experimental findings from a gas phase electron diffraction study² at 40°C (313.15 K). The data reported in ref. 2 were consistent with a conformational mixture that was unable to resolve the structure of the cyclooctane. Our MP2 results are also in agreement with an NMR study conducted at 161.5 K,⁴ where the BC conformer was found to be predominant and a CROWN family conformation was proposed to exist to a small extent (less than 6%).

Once it is established that the BC, CROWN, and in a smaller proportion, TBC, and TCC_1 conformers are the probable structures to be observed in a conformational mixture at a range of temperatures, it is certainly of interest to investigate the conformational interconversion process. Anet et al.^{4,20} proposed in previous NMR and MM studies that

TABLE III.

Ab Initio Ring Dihedral Angles and Empirical Previously Found Values for CC and TCC Conformers.

Angles and Degrees	Conformer CC Values					
	Empirical ^a	MM2 ^b	AMI ^c	HF / 3–21G ^c	Present Work	
					HF / 3–21G	HF / 6–31G*
ΔE / kcalmol ^{−1d}	0.58	1.13	−1.41	1.71	1.70	0.53 (0.53)
[C ₁ , C ₂ , C ₃ , C ₄]	−76.5	−78.9	−80.8	−79.5	−86.5	−82.8 (−83.8)
[C ₂ , C ₃ , C ₄ , C ₅]	98.6	96.1	98.3	92.7	97.9	83.4 (83.8)
[C ₃ , C ₄ , C ₅ , C ₆]	−98.6	−96.1	−98.3	−92.7	−85.0	−84.0 (−83.0)
[C ₄ , C ₅ , C ₆ , C ₇]	76.5	78.9	80.8	79.5	74.6	83.4 (83.0)
[C ₅ , C ₆ , C ₇ , C ₈]	−76.5	−78.9	−80.8	−79.5	−86.4	−82.9 (−83.8)
[C ₆ , C ₇ , C ₈ , C ₁]	98.6	96.1	98.3	92.7	98.0	83.4 (83.8)
[C ₇ , C ₈ , C ₁ , C ₂]	−98.6	−96.1	−98.3	−92.7	−85.2	−83.9 (−83.0)
[C ₈ , C ₁ , C ₂ , C ₃]	76.5	78.9	80.8	79.5	74.6	83.3 (83.0)
Conformer TCC Values						
ΔE / kcalmol ^{−1d}	0.20	0.95	−1.46	1.65	1.67	0.53 (0.53)
[C ₁ , C ₂ , C ₃ , C ₄]	63.7	63.3	69.0	62.6	69.8	83.4 (83.8)
[C ₂ , C ₃ , C ₄ , C ₅]	−85.4	−85.2	−87.6	−84.3	−85.8	−82.7 (−83.8)
[C ₃ , C ₄ , C ₅ , C ₆]	110.7	111.3	110.1	110.3	102.9	83.5 (83.0)
[C ₄ , C ₅ , C ₆ , C ₇]	−85.1	−85.1	−88.4	−84.4	−85.0	−84.2 (−83.0)
[C ₅ , C ₆ , C ₇ , C ₈]	63.7	63.3	69.0	62.6	69.9	83.4 (83.8)
[C ₆ , C ₇ , C ₈ , C ₁]	−85.4	−85.2	−87.6	−84.3	−85.8	−82.6 (−83.8)
[C ₇ , C ₈ , C ₁ , C ₂]	110.7	111.3	110.1	110.3	102.9	83.4 (83.0)
[C ₈ , C ₁ , C ₂ , C ₃]	−85.1	−85.1	−88.4	−84.4	−84.9	−84.1 (−83.0)

The HF / 6–31G* values for the CROWN conformer are given in parentheses for comparison.

^a Values from ref. 18.

^b Values from ref. 9.

^c Values from ref. 11.

^d Energy difference with relation to the BC conformer.

there is a rapid pseudorotation among the conformer members of the boat–chair family (BC \rightleftharpoons TBC) and crown family (CROWN \rightleftharpoons CC \rightleftharpoons TCC). This would lead to a single peak in the NMR spectra. In the present work, we showed that the CC and TCC conformers do not exist. Therefore, the last pseudorotation process does not take place and instead the interconversion should be considered between the CROWN and the BC and TBC (and TCC₁) conformers. The BC and TBC conformers were predicted to pseudorotate rapidly²⁰ with an energy barrier of 3.3 kcal/mol (MM value), and the experimental value was estimated to be less than 4 kcal/mol.²⁰ The empirical energy barrier was evaluated by driving a dihedral angle in an attempt to follow a minimum energy path on the multidimensional PES. In the present study we located a TS structure named TS₂ carrying out full geometry optimization, following an imaginary frequency mode,²¹ in a region of the PES that

resembles a TS structure connecting the BC and TBC conformers (see Table I). The energy difference with respect to the global minimum BC conformer is 3.04 kcal/mol (MP2/6–311G*//6–31G* value), which is in agreement with the results of the Anet et al. work. In this case a single dihedral angle driving was successful in predicting an energy barrier. It should be emphasized that our calculation employed a full symmetry unconstrained geometry optimization procedure seeking a stationary point exhibiting a single negative eigenvalue of the Hessian matrix,²¹ so the TS structure is precisely located. The BC \rightleftharpoons TBC interconversion scheme, showing the 3-dimensional structures, is depicted in Figure 3, where it can be visualized that the TS₂ structure is indeed the barrier for the conformational interconversion.

The interconversion between the TBC and TCC (actually the CROWN conformer) has been proposed²⁰ to have an energy barrier of 10.3 kcal/mol

TABLE IV.
***Ab Initio* Total Gibbs Free Energy Difference (kcal / mol) Calculated with Respect to BC Conformer**
[$\Delta G^{\text{TOT}} = \Delta G_{\text{TRANS}} + \Delta G_{\text{ROT}} + \Delta G_{\text{VIB}} + \Delta E(\text{electronic} + \text{nuclear repulsion})$] for Six True Minimum
Energy Structures on PES for Cyclooctane Molecule at Various Temperatures.

	B	BB	BC	CROWN	TBC	TCC ₁
<i>T</i> = 161.55 K						
HF/3-21G	3.995	4.571	0.0	0.764	1.620	1.623
HF/6-31G	3.974	3.990	0.0	−0.452	1.533	1.536
HF/6-31G*	3.363	3.252	0.0	−0.436	1.691	1.691
MP2/6-31G//6-31G	3.274	3.320	0.0	0.928	1.583	1.596
MP2/6-31G*//6-31G	3.254	3.370	0.0	0.858	1.743	1.736
MP2/6-31G*//6-31G*	3.213	3.182	0.0	1.024	1.741	1.741
MP2/6-311G*//6-31G*	2.943	3.182	0.0	1.254	1.621	1.621
<i>T</i> = 298 K						
HF/3-21G	3.868	4.929	0.0	0.209	1.494	1.502
HF/6-31G	3.792	3.691	0.0	−1.198	1.391	1.392
HF/6-31G*	3.007	2.781	0.0	−1.017	1.531	1.530
MP2/6-31G//6-31G	3.092	3.021	0.0	0.182	1.441	1.452
MP2/6-31G*//6-31G	3.072	3.071	0.0	0.112	1.601	1.592
MP2/6-31G*//6-31G*	2.857	2.711	0.0	0.443	1.581	1.580
MP2/6-311G*//6-31G*	2.587	2.711	0.0	0.673	1.461	1.460
<i>T</i> = 313.15 K						
HF/3-21G	3.854	4.977	0.0	0.147	1.480	1.488
HF/6-31G	3.772	3.659	0.0	−1.282	1.376	1.376
HF/6-31G*	2.969	2.730	0.0	−1.082	1.514	1.512
MP2/6-31G//6-31G	3.072	2.989	0.0	0.098	1.426	1.436
MP2/6-31G*//6-31G	3.052	3.039	0.0	0.028	1.586	1.576
MP2/6-31G*//6-31G*	2.819	2.660	0.0	0.378	1.564	1.562
MP2/6-311G*//6-31G*	2.549	2.660	0.0	0.608	1.444	1.442

The thermodynamic functions were evaluated using *ab initio* HF scaled (0.89) harmonic frequencies.

(MM value) while the experimentally estimated value is 10.5 kcal/mol.²⁰ Again the MM empirical value was obtained by driving a single dihedral angle aiming to follow the interconversion path. However, no geometrical parameters have been reported so far for any TS structure located on the PES for the cyclooctane molecule; only energy barriers have been given. We were able to locate a true TS structure (with only one negative eigenvalue of the Hessian matrix, TS₁; see Table I) that may connect the TBC (or BC) and CROWN conformers. It is well above the global minimum BC structure, having an energy difference of 11.64 kcal/mol (MP2/6-31G*//6-31G* value). Our calculated energy barrier is not so far away from the previously reported value. The conformational interconversion route is shown in Figure 4 where the TS₁ structure is situated halfway between the BC (or TBC) and CROWN conformers. Because it has been proposed that the TBC pseudorotates rapidly to the BC conformer, we assume that this interconversion involves the BC and CROWN con-

formers. The energy barrier value reported here can provide an explanation for the two peaks observed in the NMR spectra by Anet et al.⁴ The major one is assigned to the BC conformer, and the second peak is attributed to the CROWN structure. The BC and CROWN forms of the cyclooctane molecule are inverting slowly on the NMR scale, thus originating two distinct peaks. The two TS structures located in the present study provide an unambiguous and clear explanation for the experimental spectral findings regarding the cyclooctane molecule.

Conclusion

In the present article, the PES for the cyclooctane molecule was investigated using high level *ab initio* theory. Six true minimum energy structures and two TS structures, characterized via harmonic frequency analysis, were located on the PES. The

TABLE V.
Percent Concentration of Each Conformer Located on PES for Cyclooctane Molecule Evaluated from *Ab Initio*
Calculated Equilibrium Constants ($K_{eq} = \exp[-\Delta G / RT]$) / for Distinct Temperatures (see Table II).

	[B]	[BB]	[BC]	[CROWN]	[TBC]	[TCC ₁]
<i>T</i> = 161.5 K						
HF/3-21G	0.0004	0.0001	90.48	8.37	0.58	0.58
HF/6-31G	0.0001	0.0001	19.58	80.09	0.16	0.16
HF/6-31G*	0.003	0.0008	20.40	79.39	0.11	0.11
MP2/6-31G//6-31G	0.003	0.003	93.49	5.19	0.67	0.65
MP2/6-31G*//6-31G	0.004	0.003	92.77	6.40	0.41	0.41
MP2/6-31G*//6-31G*	0.004	0.005	95.24	3.92	0.42	0.42
MP2/6-311G*//6-31G*	0.010	0.005	96.80	1.94	0.62	0.62
<i>T</i> = 298 K						
HF/3-21G	0.078	0.013	53.65	37.70	4.31	4.25
HF/6-31G	0.019	0.023	11.43	86.35	1.09	1.09
HF/6-31G*	0.093	0.14	14.85	82.67	1.12	1.03
MP2/6-31G//6-31G	0.28	0.32	52.05	38.29	4.57	4.49
MP2/6-31G*//6-31G	0.28	0.28	50.66	41.93	3.40	3.45
MP2/6-31G*//6-31G*	0.49	0.63	61.33	29.03	4.25	4.26
MP2/6-311G*//6-31G*	0.84	0.68	66.05	21.21	5.61	5.62
<i>T</i> = 313.15 K						
HF/3-21G	0.10	0.017	50.60	39.96	4.69	4.63
HF/6-31G	0.026	0.031	11.02	86.51	1.21	1.21
HF/6-31G*	0.14	0.21	16.99	96.66	1.49	1.50
MP2/6-31G//6-31G	0.35	0.40	48.30	41.26	4.88	4.81
MP2/6-31G*//6-31G	0.35	0.36	46.98	44.91	3.67	3.73
MP2/6-31G*//6-31G*	0.62	0.80	57.75	31.46	4.68	4.69
MP2/6-311G*//6-31G*	1.04	0.87	62.36	23.47	6.12	6.14

The sum of the concentrations was assumed to be unity.

minimum energy structures reported here are the possible conformations of the cyclooctane molecule. Some previous reported AM1 and HF/3-21G structures appear to be artifacts of less accurate quantum mechanical calculations. Two TS structures connecting minima on the PES are reported for the first time in the literature, along with barriers for conformational interconversions calculated using the MP2 treatment of electron correlation. *Ab initio* calculated energy differences and harmonic frequencies were used for the evaluation of total Gibbs free energy change values, which allowed the determination of equilibrium constants as a function of the temperature. Our *ab initio* MP2 results showed that at low temperature the BC conformer is predominant and above room temperature there is a conformational mixture of ca. 66% of the BC and ca. 21% of the CROWN conformers (MP2/6-311G*//6-311G* values). Our theoretical results are in good agreement with the gas phase electron diffraction study at 300 K and

an NMR study in solution at 161.5 K that predicted the BC conformer as the predominant form of the cyclooctane molecule. The conformational interconversion between the BC, TBC, and CROWN conformers was also investigated. The calculated energy barriers for the BC \rightleftharpoons TBC and BC \rightleftharpoons CROWN interconversions are, respectively, 3.04 and 11.64 kcal/mol (MP2/6-311G*//6-31G* values). These results are in agreement with the previously reported empirical values and with the NMR predictions of the pseudorotation process and spectral assignments. Finally, the present study showed that care is needed when using empirical, semiempirical, and HF level of theory in conformational analysis studies involving cyclic compounds. The HF level of theory in conjunction with extended basis sets produced consistent geometrical parameters; however, an adequate treatment of electron correlation is required for evaluating *ab initio* relative energies and conformational populations at a range of temperatures.

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References

1. J. B. Henrickson, *J. Am. Chem. Soc.*, **89**, 7047 (1967).
2. A. Almenningen, O. Bastiansen, and H. Jensen, *Acta Chem. Scand.*, **20**, 2689 (1966).
3. M. Dobler, J. D. Dunitz, and A. Mugnol, *Helv. Chim. Acta*, **49**, 2492 (1966).
4. F. A. L. Anet and V. J. Basus, *J. Am. Chem. Soc.*, **95**, 4424 (1973).
5. P. W. Pakes, T. C. Rounds, and H. L. Strauss, *J. Phys. Chem.*, **85**, 2476 (1981).
6. O. V. Dorofeeva, V. S. Mastryukov, K. Siam, J. D. Ewbank, N. L. Allinger, and L. Schaefer, *J. Struct. Chem.*, **31**, 153 (1990) [Original (Russian) *Zhu. Strukt. Khim.*, **31**, 167 (1990)].
7. M. Saunders, *J. Am. Chem. Soc.*, **109**, 3150 (1987).
8. (a) M. Lipton and W. C. Still, *J. Comput. Chem.*, **9**, 343 (1988); (b) G. Chang, W. C. Guida, and W. C. Still, *J. Am. Chem. Soc.*, **111**, 4379 (1989).
9. D. M. Ferguson and D. J. Raber, *J. Am. Chem. Soc.*, **111**, 4371 (1989).
10. D. J. Brecknell, D. J. Raber, and D. M. Ferguson, *J. Mol. Struct.*, **124**, 343 (1985).
11. D. M. Ferguson, I. R. Gould, W. A. Glauser, S. Schroeder, and P. A. Kollman, *J. Comput. Chem.*, **13**, 525 (1992).
12. The MMX force field is derived from the MM2 (QCPE-395, 1977) force field of N. L. Allinger, and the pi-VESCF routines are taken from MMP1 (QCPE-318), also developed by N. L. Allinger. This force field with the random search routine is implemented in the PCMODEL software available from Serena Software, PO Box 3076, Bloomington, IN 47402-3076.
13. S. Huzinaga, J. Andzelm, M. Klobukowski, E. Radzio-Andzelm, Y. Sakai, and H. Tatewaki, In: *Gaussian Basis Sets for Molecular Calculations*, Elsevier, Amsterdam, 1984.
14. (a) R. Ditchfield, W. J. Hehre, and J. A. Pople, *J. Chem. Phys.*, **54**, 724 (1971); (b) W. J. Hehre, R. Ditchfield, and J. A. Pople, *J. Chem. Phys.*, **56**, 2257 (1972).
15. W. R. Rocha and W. B. De Almeida, *J. Comput. Chem.*, **18**, 254 (1997).
16. R. Krishnan, J. S. Binkley, R. Seeger, and J. A. Pople, *J. Chem. Phys.*, **72**, 650 (1980).
17. M. W. Schmidt, K. K. Baldridge, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. H. Jensen, S. Kosek, N. Matsunaga, K. A. Nguyen, S. J. Su, T. L. Windus, M. Dupuis, and J. A. Montgomery, *J. Comput. Chem.*, **14**, 1347 (1993).
18. P. W. Pakes, T. C. Rounds, and H. L. Strauss, *J. Phys. Chem.*, **85**, 2469 (1981).
19. J. A. Pople, A. P. Scott, M. W. Wong, and L. Radom, *Israel J. Chem.*, **33**, 345 (1993).
20. F. A. L. Anet and J. Krane, *Tetrahedron Lett.*, **50**, 5029 (1973).
21. (a) P. Culot, G. Dive, V. H. Nguyen, and J. M. Ghuysen, *Theor. Chim. Acta*, **82**, 189 (1992); (b) J. M. Bofil, *J. Comput. Chem.*, **15**, 1 (1994).